

Global Economic Burden of Congenital Cytomegalovirus: A Systematic Literature Review

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BACKGROUND

- Cytomegalovirus (CMV) is a common pathogen that can infect individuals regardless of age; following primary infection, reactivation of latent virus and/or reinfection with a different strain can occur¹
- While healthy individuals with CMV infection typically have no symptoms or experience mild illness, CMV can be transmitted from a pregnant woman to her fetus during pregnancy, causing congenital CMV (cCMV) in the newborn^{1,2}
- cCMV is the most frequent infectious cause of congenital birth defects and is a leading cause of sensorineural hearing loss and neurodevelopmental disability³
 - In the United States and Europe, 0.5%–1% of babies are born with cCMV infection⁴
 - Approximately 10% of newborns with cCMV infection are symptomatic at birth; 40%–60% of these newborns will have long-term sequelae²
 - Approximately 10%–15% of newborns who are asymptomatic at birth will develop long-term sequelae⁵
- Treatment of cCMV is limited; there are no vaccines available to protect against infection of the fetus during pregnancy
- Characterization of the economic costs of cCMV is necessary to better understand the financial burden that cCMV can place on healthcare systems and families, as well as to evaluate the financial impact of prevention strategies

OBJECTIVE

- To describe the global economic burden of cCMV in newborns, infants, and children from 2010–2020 by performing a systematic literature review

METHODS

Search Strategy

- A broad systematic literature search for CMV-related economic burden was initially conducted
 - Data sources: bibliographic databases (Medline, Embase, and LILACS) and congresses; English language only
 - Search time frame: 2010 to 2020 for journal articles and 2017 to 2020 for congress materials
 - Population: all age groups, mothers and infants with HIV, and specific subpopulations or immunocompromised groups
 - Geographic locations: Australia, Latin America, Canada, Europe, Israel, Japan, the United States, and multiple regions
- From this broad literature search, specific estimates of the economic burden related to cCMV were extracted for this presentation
 - Inclusion criteria
 - Population: newborns (≤ 1 month of age), infants (2 months to 2 years of age), and children (3–10 years of age)
 - Geographic locations: Europe, Canada, and the United States
 - Results: direct costs and healthcare resource utilization (HCRU)
 - Exclusion criteria
 - Publication type: congress abstracts and presentations

Outcome

- cCMV-attributable direct costs and HCRU (hospitalization-related)

RESULTS

Identified Studies

- Overall, 751 records on CMV-related economic burden were initially identified, duplicates were removed, and 573 records were screened (**Figure 1**)
 - In total, 538 records were excluded during screening and full-text review based on study population, outcome, design, or other reasons
- A total of 35 reports were included in the data extraction stage
 - Of the extracted studies for the overall CMV economic burden review, 11 reported cCMV-attributable direct costs or HCRU in newborns, infants, or children in Europe, Canada, or the United States and are included in this presentation

Geographic Distribution of Studies

- Studies reporting direct costs and HCRU (n = 11) included data from the following countries or regions (**Figure 2**):
 - Studies reporting direct costs were conducted in the United States (n = 5), the United Kingdom (n = 1), and the Netherlands (n = 1)
 - Studies reporting HCRU were conducted in the United States (n = 4), Poland (n = 1), England (n = 1), and the Netherlands (n = 1)

Figure 1. Study Selection for Economic Burden

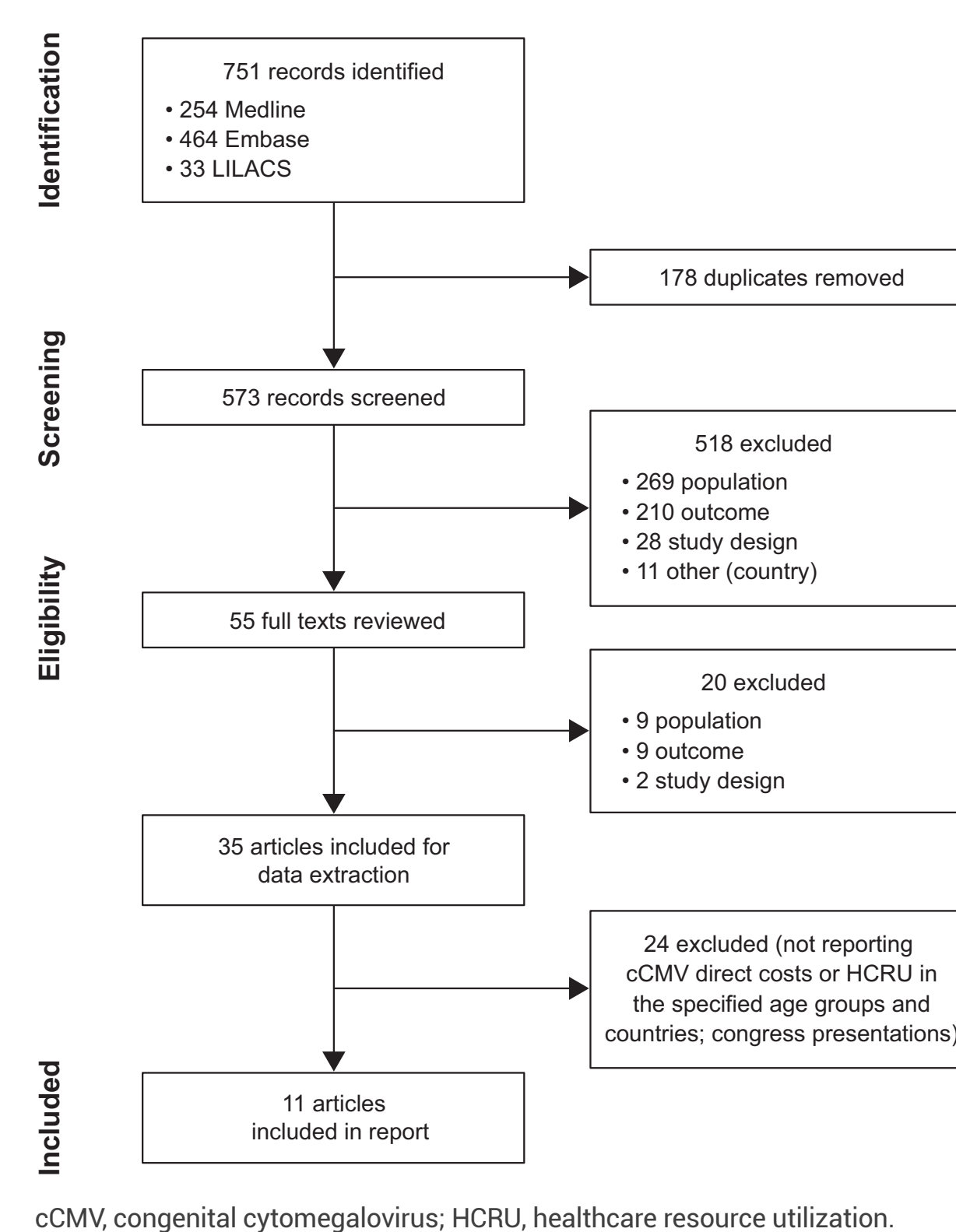
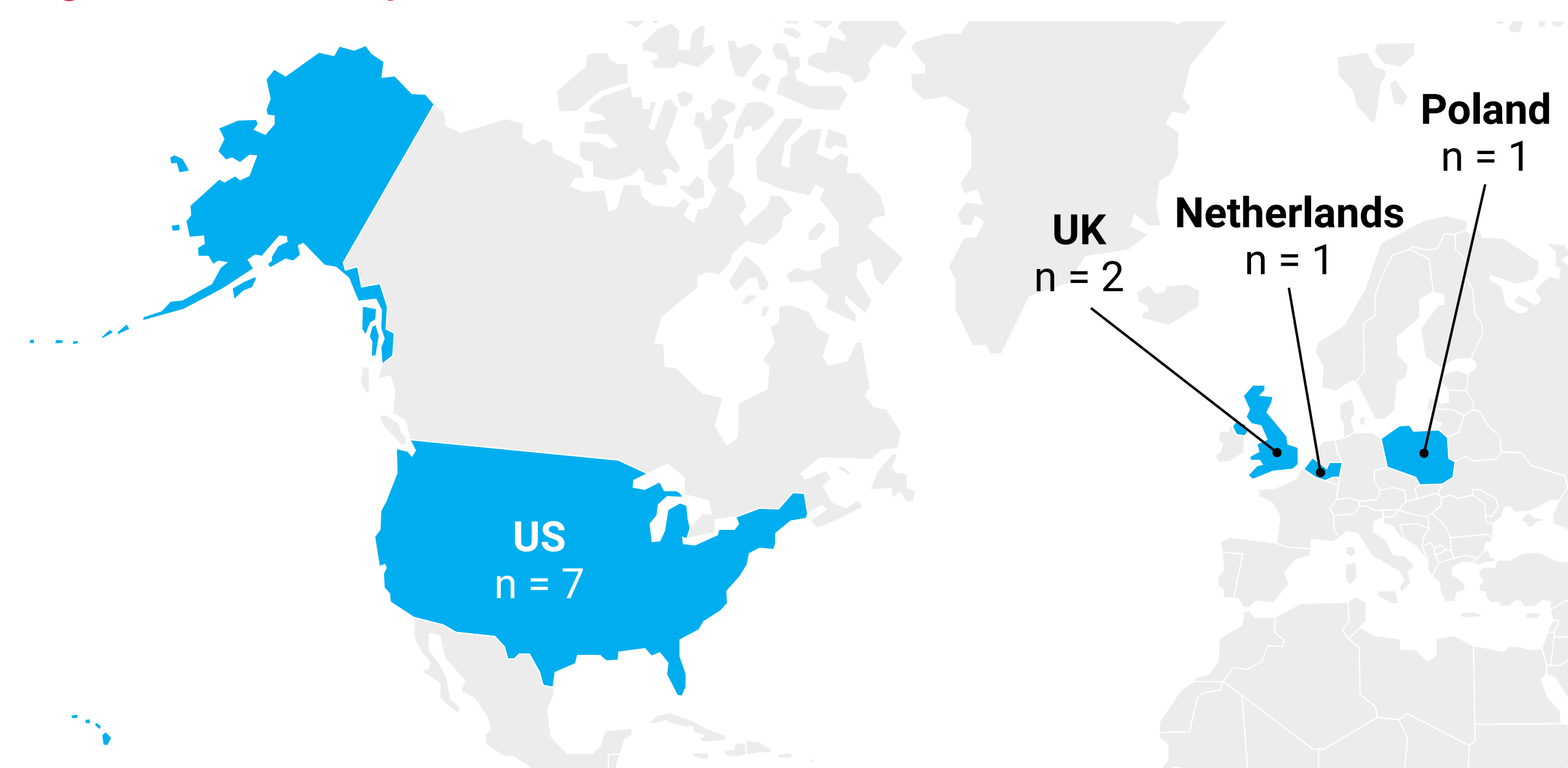


Figure 2. Global Map of the Location and Number of Included Studies



Summary of Direct Costs and HCRU

- cCMV-related direct costs and HCRU were reported in 7 studies each (**Tables 1 and 2**)
 - Direct costs in the United States among infants with cCMV were up to \$108,000 per hospitalization
 - The length of cCMV-related hospital stays among newborns, infants, and children ranged from 5–99 days in the United States and 6–38 days in Europe (Poland)

Table 1. Summary of Included Studies Reporting cCMV-related Direct Costs (n = 7)

Study	Study Design	Country	Study Period	Currency	Population and Sample Size	Direct Costs Related to cCMV*			
						Lowest Cost Reported		Highest Cost Reported	
						Category	Cost	Category	Cost
Williams EJ, et al. <i>Arch Dis Child Fetal Neonatal Ed.</i> 2015. DOI: 10.1136/archdischild-2014-306756	Cost analysis	United Kingdom	2010–2011	GBP	Asymptomatic infants with cCMV (n = NR)	Salivary testing	£19	Total cost of identifying (screening plus initial assessment), treating, and following up cases	£6683*
Korndewal MJ, et al. <i>Arch Dis Child.</i> 2018. DOI: 10.1136/archdischild-2017-312805	Retrospective cohort	Netherlands	2012–2013	Euro	Children with cCMV (n = 133)	Attendance at a speech and hearing center (mean)	82 €	Total costs per child (mean)	17,205 €
Gantt S, et al. <i>JAMA Pediatr.</i> 2016. DOI: 10.1001/jamapediatrics.2016.2016	Cost-effectiveness analysis	United States	2014–2016	USD	Newborns ^c (n = NR)	Cost per test for collection and CMV PCR testing of oral swab of all screened newborns	\$10–50	Total annual cost per patient 6 to <13 years, severe to profound	\$20,771
Lucas A, et al. <i>Cost Eff Resour Alloc.</i> 2019. DOI: 10.1186/s12962-019-0189-0	Conceptual framework	United States	2019	USD	Infants with cCMV (n = NR)	Cost per hospitalization birth only, vaginal (mean)	\$25,203	Cost per hospitalization, <1 year including birth (mean)	\$107,744
Inagaki K, et al. <i>J Pediatr.</i> 2018. DOI: 10.1016/j.jpeds.2018.03.036	Retrospective analyses of serial cross-sectional data	United States	2000, 2003, 2006, 2009, 2012	USD	Infants with symptomatic cCMV; birth year 2000 (n = 221), birth year 2003 (n = 222), birth year 2006 (n = 235), birth year 2009 (n = 327), birth year 2012 (n = 344), general (n = 1349)	Total charge per case, birth year 2000 (2012 USD)	\$45,771	Total charge per case, birth year 2006 (2012 USD)	\$89,846
Bergevin A, et al. <i>Int J Pediatr Otorhinolaryngol.</i> 2015. DOI: 10.1016/j.ijporl.2015.09.019	Economic estimation	United States	2014, 2015	USD	Infants (n = NR)	CMV screening program setup	\$4000	Total costs	\$57,348
Myers JM, et al. <i>Clin Ther.</i> 2019. DOI: 10.1016/j.clinthera.2019.04.022	Retrospective analysis of health insurance claims data	United States	2011–2016	USD	Infants with symptomatic cCMV; birth analysis vaginal delivery (n = 170), birth analysis cesarean delivery (n = 234), post-birth analysis (n = 679)	Unadjusted cCMV disease-related health care costs	\$23,614	Overall costs of birth (median; birth analysis cesarean delivery)	\$98,126

cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; DOI, digital object identifier; GBP, British pound sterling; NR, not reported; PCR, polymerase chain reaction; USD, United States dollar.

*Range includes the lowest and highest direct cost across the specific categories reported in the study.

^cCost per single case of cCMV-related sensorineural hearing loss identified; total cost per 100,000 infants undergoing newborn hearing screening program, £113,615.

^dNewborns include symptomatic newborns with cCMV infection and/or hearing loss at birth, all newborns with cCMV infection, all treated newborns, all screened newborns, and all newborns with cCMV infection without hearing loss at birth.

Table 2. Summary of Included Studies Reporting cCMV-related HCRU (n = 7)

Study	Study Design	Country	Study Period	Population and Sample Size	cCMV-related HCRU: Length of Hospital Stay*				cCMV-related HCRU: Other Hospitalization Outcomes ^b
					Lowest		Highest		
					Category	Number of Days	Category	Number of Days	
Jedlińska-Pijanowski D, et al. <i>Adv Clin Exp Med.</i> 2020. DOI: 10.17219/acem/125427	Retrospective	Poland	2012–2017	Symptomatic cCMV neonates on antiviral treatment; general (n = 98), GCV-based therapy (n = 60), 2012 (beginning of the study; n = 31), 2017 (end of the study; n = 35)	Oral VGCV monotherapy	6	GCV monotherapy	38	NR
Kadambari S, et al. <i>Lancet Infect Dis.</i> 2020. DOI: 10.1016/S1473-3099(19)30416-5	Population-based observational study	England	1968–2016	Infants (n = NR)	NR	NR	NR	NR	Percentage of patients discharged from hospital ranged from 4.6%–22.7%
Korndewal MJ, et al. <i>Arch Dis Child.</i> 2018. DOI: 10.1136/archdischild-2017-312805	Retrospective cohort	Netherlands	2012–2013	Children with cCMV (n = 133)	Children with cCMV	8.1	Children with cCMV	8.1	Percentage of patients admitted to hospital was 45.9% for pediatric and 13.5% for neonates
Tran CL, et al. <i>Am J Perinatol.</i> 2020. DOI: 10.1055/s-0039-1683958	Retrospective analysis of NICU database	United States	2005–2010	Infants; VLBW infants with cCMV (n = 174), infants >1500 g with cCMV (n = 145)	Infants >1500 g with cCMV	61	VLBW infants with cCMV	98	NR
Inagaki K, et al. <i>J Pediatr.</i> 2018. DOI: 10.1016/j.jpeds.2018.03.036	Retrospective analyses of serial cross-sectional data	United States	2000, 2003, 2006, 2009, 2012	Infants with symptomatic cCMV; birth year 2000 (n = 221), birth year 2003 (n = 222), birth year 2006 (n = 235), birth year 2009 (n = 327), birth year 2012 (n = 344), general (n = 1349)	Birth year 2000	15	Birth year 2006	27	NR
Lanzieri TM, et al. <i>J Perinat Med.</i> 2014. DOI: 10.1515/jpm-2013-0183	Retrospective review of medical database	United States	2005–2010	Infants with CMV infection; VLBW infants (n = 87), infants >1500 g (n = 69)	Infants >1500 g with CMV infection	48	VLBW infants with CMV infection	99	NR
Myers JM, et al. <i>Clin Ther.</i> 2019. DOI: 10.1016/j.clinthera.2019.04.022	Retrospective analysis of health insurance claims data	United States	2011–2016	Infants with symptomatic cCMV; birth analysis vaginal delivery (n = 170), birth analysis cesarean delivery (n = 234), post-birth analysis (n = 679)	Post-birth analysis	5	Birth analysis cesarean delivery	37.5	Percentage of patients admitted to the hospital with a cCMV-related inpatient admission was 7.5%

cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; DOI, digital object identifier; GCV, ganciclovir; HCRU, healthcare resource utilization; NR, not reported; NICU, newborn intensive care unit; VGCV, valganciclovir; VLBW, very low birth weight.

*Range includes the lowest and highest number of hospitalization days reported in the study.

^bOther hospitalization outcomes apart from length of stay included admission, readmission, discharge, and frequency.

CONCLUSIONS

- There is a lack of consistent data on the economic burden of cCMV worldwide, with a great deal of heterogeneity among existing studies and regions
 - However, the economic impact of cCMV appears substantial and remains a key consideration when assessing the value of cCMV interventions and prevention strategies, such as vaccines
- Additional country-level research is needed to further quantify the burden of cCMV disease, including direct and indirect economic costs

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Disclosures

- JD-D, AN, CT, and PB are employees of Moderna, Inc. and hold stock/stock options in the company. JM, MN, MK, and ES are employees of and WL was an employee of Certara, Inc., were consultants for Moderna, Inc., and were paid for their services. EM has nothing to disclose.

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